AF

PATENT
Attorney Docket No. 09210.0004

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
Burton G. CHRISTENSEN et al.	)	Group Art Unit: 1639
	)	
Application No.: 09/457,926	)	Examiner: Mark Shibuya
	)	
Filed: December 8, 1999	)	
	)	
For: NOVEL ANTIBACTERIAL AGENTS	)	Confirmation No.: 8221

Attention: Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

REPLY BRIEF UNDER 37 C.F.R. § 41.41

Pursuant to 37 C.F.R. § 41.41, Appellants presents this Reply Brief in response to the Examiner's Answer dated November 15, 2006. Appellant also filed a Request for Oral Hearing concurrently herewith.

If there are any fees due in connection with the filing of this Reply Brief that are not enclosed herewith, please charge such fees to our Deposit Account No. 06-0916.

I. INTRODUCTION

Appellants submit this Reply Brief to address several erroneous assertions set forth in the Examiner's Answer.[1] More specifically, despite maintaining the rejection of claims 41, 43, 49-51, and 53-55 under 35 U.S.C. § 103(a) over Truett I in view of Truett II, Boeckh, Renoud-Grappin, and Staroske, the Office failed to identify where in the prior art there is a "motivation,

[1] Appellants have endeavored to address assertions in the Examiner's Answer without unduly repeating the same arguments in Appellants' Opening Brief.

suggestion or teaching of the desirability of making **the specific combination** that was made by the applicant." *In re Kotzab*, 217 F.3d 1365, 1370, 55 U.S.P.Q.2d 1313, 1316 (Fed. Cir. 2000) (emphasis added). Instead, the Office once again bases its obviousness rejection on the general goal or desire to obtain a broad spectrum antibiotic while ignoring the teachings of the cited references as a whole. For the reasons presented here and in Appellants' Opening Brief, the Office's 35 U.S.C. § 103 rejection is improper and should be reversed

II. ARGUMENT IN REPLY

A. The Office Cannot Modify the Art in a Manner That Would Destroy the Intended Function of the Disclosed Compounds

In its Opening Brief, Appellants argued that Truett II discloses a three-antibiotic compound consisting of ceftazidime, a quinolone, and vancomycin, and that by eliminating the quinolone to obtain the presently claimed invention, as suggested by the Office, the intended function of the three-antibiotic compound disclosed in Truett II would be destroyed. *See* Opening Brief at 11-13. In response, the Office states:

> appellant has not provided evidence or reasons as to why an obvious dimeric antibiotic composition of a beta lactam and a vancomycin would represent a modification to the trimeric antibiotic composition of Truett II such that the antibiotic composition would not work for its intended purpose.

Examiner's Answer at 16. The Office's contention, however, has no basis in fact once Truett II is considered as a whole.

To begin with, the Office has impermissibly shifted the burden of persuasion to Appellants. It is the Office that must establish a *prima facie* case of obviousness, which includes establishing that "[t]he references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination." *See* M.P.E.P. § 2141 (citing *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 n. 5, 229 U.S.P.Q. 182, 187 n. 5

(Fed. Cir. 1986)). This the Office has not done. When all of the cited references are considered as a whole, they suggest the combination of ceftazidime and vancomycin in only two ways—as part of a three-antibiotic composition (Truett II) or as a mixture of the two, but not joined by a linker (Boeckh). Truett I, Renoud-Grappin, and Staroske teach nothing more than the concept of linking compounds together. But none of these references suggest joining ceftazidime with vancomycin via a linker.

Moreover, Appellants have provided ample evidence that modification of Truett II's "trimeric" antibiotic composition, by eliminating the quinolone to form the dimeric antibiotic composition of the presently claimed invention, would destroy the intended function of the disclosed compounds. For instance, Truett II explicitly states throughout that the "value" of the disclosed compositions resides in the "trio" of antibiotics. *See* Truett II at col. 1, lines 22-31. The only example in Truett II is directed to the three-component antibiotic. *Id.* at col. 24, line 50 to col. 25, line 43. And Truett II specifically directs one of skill in the art to add a third antibiotic, such as vancomycin, to the "bi-component" composition. *Id.* at col. 1, lines 16-21. Even the Office acknowledges that the "value" in Truett II's compositions is derived from the three-antibiotic combination. *See* Examiner's Answer at 16. These statements establish that the success of Truett II's compositions is due to its three-component structure.

The Office has not provided any evidence, other than an unsupported generalized statement, that one of skilled in the art would consider a two-antibiotic compound to work as intended by Truett II's three-antibiotic compound. There is simply no teaching provided in Truett II, or any of the other cited references, that the combination of ceftazidime and vancomycin would lead to the results disclosed in Truett II. *In re Fritch*, 972 F.2d 1260, 1265 n.12, 23 U.S.P.Q.2d 1780, 1783 n. 12 (Fed. Cir. 1992) ("A proposed modification [is]

inappropriate for an obviousness inquiry when the modification render[s] the prior art reference inoperable for its intended purpose."); *In re Ratti*, 270 F.2d 810, 813, 123 U.S.P.Q. 349, 352 (C.C.P.A. 1959) (holding the suggested combination of references improper under § 103 because it "would require a substantial reconstruction and redesign of the elements shown in [a prior art reference] as well as a change in the basic principles under which [that reference's] construction was designed to operate").

In an attempt to rebut this conclusive evidence, the Office contends that:

> the value of the disclosed composition is that the bacterial infective agent will be simultaneously attacked by the linked trio of agents which are known to attack the cell-wall producing enzyme of the bacteria, and that emergence of resistance against the antibiotics will be prevented.
>
> These same "values", which the examiner respectfully submits are tantamount to uses or functions, are also attributed to composition that are made by linking two antibiotic moieties, as taught by the prior art.

Examiner's Answer at 16. But the Office's response is nothing more than a generalized goal for any antibiotic compound—attacking the bacteria and prevent antibiotic resistance. This general goal, however, is insufficient to support a *prima facie* case of obviousness, which requires a suggestion or motivation to make the specific combination made by the Appellants. *In re Kotzab*, 217 F.3d at 1370, 55 U.S.P.Q.2d at 1316. Moreover, the Office cannot rely on a general desire in the art to obtain a broad spectrum antibiotic but ignore the teachings of Truett II, which teach achieving this goal with a three-antibiotic compound.

The Office also relies on Renoud-Grappin's and Truett I's general teaching that linking compounds can be of value. *See* Examiner's Answer at 17-18. But these references fail to motivate one of skill in the art to link ceftazidime with vancomycin and, more importantly, the

references certainly would not motivate one to conduct a substantial reconstruction and redesign of the three-antibiotic compositions disclosed in Truett II. *See In re Fritch*, 972 F.2d at 1265 n.12, 23 U.S.P.Q.2d at 1783 n. 12; *In re Ratti*, 270 F.2d at 813, 123 U.S.P.Q. at 352.

Finally, the Office asserts that "one of skill in the art would not find that the dimeric compound of the *primary* reference of Truett I, would be rendered inoperable by the modification of substituting a vancomycin compound into the dimeric compound." *Id.* at 18 (emphasis in original). The problem, however, is that none of the references teach, suggest, or motivate one of skill in the art to replace a component of Truett I with vancomycin. Truett I does disclose two-antibiotic compositions, but none containing vancomycin. Boeckh discloses the use of ceftazidime in a mixture with vancomycin, but not as a linked compound (Boeckh at 92), and Truett II, the same inventor as Truett I, discloses the combination of ceftazidime and quinolone with the option of adding vancomycin to this two-antibiotic composition. Considering these references as a whole, as the Office must do, there is simply no motivation to eliminate the quinolone from Truett II's composition or replace a compound in Truett I's composition with vancomycin.

B. Truett II Does Teach Away From the Claimed Invention

Contrary to the Office's position (Examiner's Answer at 19-20), Truett II does teach away from making a two-component antibiotic consisting of ceftazidime and vancomycin. This is particularly true when one considers the fact that Truett II and Truett I are from the same inventor—that is, when all of the references are considered as a whole.

The only two-component antibiotic disclosed in Truett II consists of linking a quinolone antibiotic to a beta-lactam antibiotic such as ceftazidime. Thus, if one of skill in the art were

motivated to make a two-component antibiotic, that compound would not contain vancomycin. And if a three-component antibiotic were made, that compound would include vancomycin only if a quinolone and ceftazidime were also present. Moreover, in Truett I, which also discloses two-antibiotic compositions, inventor Truett never discloses, let alone suggests, linking ceftazidime to vancomycin. These references specifically teach away from a two-antibiotic composition consisting of ceftazidime and vancomycin.

The Office further contends that "the linked antibiotics of Truett II are structurally similar to the instant compound." *Id.* at 19. The Office is wrong. As discussed above, Truett II discloses a three-component antibiotic. In the claimed invention, there are only two antibiotics joined together by a linker group. Appellants contend that a compound consisting of three antibiotics is not structurally similar to a composition consisting of only two antibiotics.

C. The Office's Obviousness Rejection Is Based on Hindsight Reasoning

The Office has not adequately addressed Appellants' contention that the selection of ceftazidime out of the 69 compounds disclosed in Truett I was based on hindsight reasoning. The Office asserts that the selection of ceftazidime is not "an unreasonable or arbitrary choice . . ." given the "guidance provided by Truett I, in its disclosed classification of antibiotics based upon a ***common molecular structure***." Examiner's Answer at 22 (emphasis added). But the Office has not explained how Truett I's alleged guidance to select an antibiotic based on "common molecular structure" directs one skilled in the art to select ceftazidime. In fact, the Office's statement that "there were a multitude of microbial agents at the time of the claimed invention" only supports Appellants' argument that the Office selected ceftazidime from the "multitude of microbial agents" only after considering Appellants' invention.

Taking into consideration only the cephalosporins disclosed in Truett I, this class of antibiotics still consists of 17 compounds, all with a common molecular structure. Truett I at col. 2, line 59 - col. 3, line 14. Based on the Office's logic, Truett I, at most, would provide guidance to select these 17 compounds. But Truett I must be considered as a whole. *See Hodosh*, 786 F.2d at 1143 n.5, 229 U.S.P.Q.2d at 187 n.5; M.P.E.P. § 2141. When considered as a whole, Truett I discloses nine classes of antibiotic compounds wherein the compounds of each class share a common molecular structure. And within these nine classes, Truett I discloses 69 individual compounds. Even if one were to assume for arguments sake that "common molecular structure" provides guidance, Truett I still fails to motivate one of skill in the art to select cephalosporins from the nine classes (and 69 compounds) disclosed and then further select ceftazidime from the 17 other cephalosporins disclosed in the reference. It is only with Appellants' application in hand that the Office was able to select ceftazidime. As such, it is clear that the Office's § 103 rejection is impermissibly based on hindsight reasoning.

D. Boeckh, Renoud-Grappin, and Staroske Do Not Provide The Requisite Motivation to Combine

The Office contends that one of skilled in the art would be motivated to combine ceftazidime and vancomycin because Boeckh discloses that "vancomycin is used in combination with ceftazidime as a broad spectrum treatment for gram positive and gram negative bacterial infections[,]" Truett I discloses that two antibiotic moieties (one that attacks gram positive and one that attacks gram negative bacteria) can be linked, and Truett II discloses the linkage of "ceftazidime, with vancomycin as part of a heterotrimeric compound, which also includes quinolone." Examiner's Answer at 23. The Office's argument fails because Boeckh teaches that the combination of ceftazidime and vancomycin, as a mixture as opposed to a linked

composition, shows "excellent clinical response . . . ." Boeckh at 94, right column. Given the lack of any disadvantage of using a mixture of ceftazidime and vancomycin, one of skill in the art would not be motivated to link the two compounds. *See Winner Int'l Royalty Cor v. Wang*, 202 F.3d 1340, 1349, 53 U.S.P.Q.2d 1580, 1587 (Fed. Cir. 2000).

In an attempt to circumvent Appellants' argument, the Office contends that Boeckh "does not stand for the proposition that the combination cocktail of ceftazidime and vancomycin is perfected to the degree such that one of ordinary skill would not be motivated to modify the composition of Boeckh." Examiner's Answer at 25. To support this contention, the Office quotes from the first paragraph of the reference. *Id.* The first paragraph of Boeckh, however, simply sets forth the basis for studying the "pharmacokinetics and serum bacterial activity of vancomycin-ceftazidime." Boeckh at 92, left column. This paragraph does not indicate that the effectiveness of a vancomycin and ceftazidime mixture has not been adequately studied, as offered by the Office, but rather that ***because of*** the known effectiveness of the combination of the two compounds in a mixture, the pharmacokinetics of such a combination need to be evaluated. *Id.* This statement would not motivate one of skill in the art to link the two compounds. Rather, given the positive results obtained in Boeckh, one skilled in the art would be motivated to continue to use vancomycin and ceftazidime in a mixture as opposed to a linked two-component antibiotic.

With respect to Renoud-Grappin, Appellants do not contest that the reference suggests linking compounds, but those compounds are anti-virals, not antibiotics. Moreover, the Office has failed to point to any disclosure in Renoud-Grappin that linking two compounds, as opposed to mixing them together as in Boeckh, leads to an improved result. Thus, when considering the

prior successful use of ceftazidime in a mixture with vancomycin as disclosed in Boeckh, Renoud-Grappin provides no motivation to link the two compounds.

Finally, the Office again asserts that Staroske suggests the use of "homodimers" of linked vancomycin to create more potent antibiotics. *See* Examiner's Answer at 24. But Staroske's disclosure of a vancomycin-vancomycin antibiotic does not provide any motivation to create a two-antibiotic composition consisting of ceftazidime joined to vancomycin by a linker.

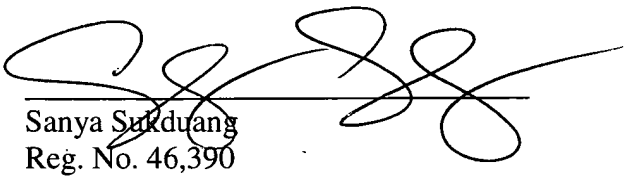
III. Conclusion

For the reasons set forth above and in Appellants' Opening Brief, the Office's rejections under 35 U.S.C. §103 are improper and should be reversed.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: January 11, 2006

By: 

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